No new matter has been added. Claims 1-15, 17-24, and 26-39 are active in this application.

REMARKS

At the outset, Applicants' representative wishes to thank Examiner Zucker and Supervisory Examiner Richter for the helpful and courteous discussion held with them on December 12, 2002, during which the prosecution of the above-identified application was materially advanced. The following remarks will expand and summarize the issues discussed.

Present Claims 1, 2, 4-15, 17-21, 29, 30, and 33-35 relate to various methods for producing N-[N-[3-(3-methoxy-4-hydroxyphenyl)propyl]-L-α-aspartyl]-L-phenylalanine 1-methyl ester, comprising:

(1) subjecting N-L-α-aspartyl-L-phenylalanine 1-methyl ester and 3-(3-methoxy-4-hydroxyphenyl)propionaldehyde or a derivative thereof to reductive alkylation in a solvent to obtain N-[N-[3-(3-methoxy-4-hydroxyphenyl)propyl]-L-α-aspartyl]-L-phenylalanine 1-methyl ester; and

(2) crystallizing said N-[N-[3-(3-methoxy-4-hydroxyphenyl)propyl]-L-α-aspartyl]-L-phenylalanine 1-methyl ester,

wherein said reductive alkylation comprises catalytic hydrogenation, and

wherein said derivative thereof is selected from the group consisting of

3-(3-methoxy-4-hydroxyphenyl)-2-propenylaldehyde,

3-(3-methoxy-4-protected-hydroxyphenyl)propionaldehyde,

3-(3-methoxy-4-protected-hydroxyphenyl)-2-propenylaldehyde, and

acetals derived therefrom.

Present Claims 23 and 26 relate to crystalline N-[N-[3-(3-methoxy-4-hydroxyphenyl)propyl]-L-α-aspartyl]-L-phenylalanine 1-methyl ester produced by such a process. Present Claims 27 and 28 relate to certain sweetening agents which contain such crystalline N-[N-[3-(3-methoxy-4-hydroxyphenyl)propyl]-L-α-aspartyl]-L-phenylalanine 1-methyl ester.

Present Claims 3, 22, 31, 32, 34, and 36-39 relate to methods for for purifying N-[N-[3-(3-methoxy-4-hydroxyphenyl)propyl]-L-α-aspartyl]-L-phenylalanine 1-methyl ester, which comprises:

subjecting a composition which comprises N-[N-[3-(3-methoxy-4-hydroxyphenyl)propyl]-L-α-aspartyl]-L-phenylalanine 1-methyl ester and at least one compound selected from the group consisting of N-L-α-aspartyl-L-phenylalanine 1-methyl ester, a peptide derivative, an amino acid, an amino acid derivative, an aldehyde, an acetal and an alcohol derivative as impurity to at least any one of the following crystallization processes:

a. crystallization with a crystallization solvent;

b. crystallization after extraction with water; and

c. when said composition comprises N-L-α-aspartyl-L-phenylalanine 1-methyl ester, further crystallization after said N-L-α-aspartyl-L-phenylalanine 1-methyl ester has been separated,

to obtain crystalline N-[N-[3-(3-methoxy-4-hydroxyphenyl) propyl]-L-α-aspartyl]-L-phenylalanine 1-methyl ester.

The cited references contain no disclosure or suggestion of such a granulated sweetener. Moreover, these references contain no teaching which would instill a reasonable expectation of success for the presently claimed methods into one of skill in the art. Accordingly, these references cannot affect the patentability of the present claims.

The rejection of Claims 1-6, 8, 9, 13, 14, 16, 19, 21, 22, 31, 32, 34, 35, 38, and 39 under 35 U.S.C. § 103(a) in view of U.S. Patent No. 5,480,668 (Nofre et al) has been obviated by appropriate amendment. As explained during the above-note interview, Nofre et al discloses, at column 6, lines 44-50, the preparation of certain compounds by condensing Aspartame:

> with an aldehyde or ketone compound which is a precursor of the group R. The intermediate imine formed by condensation is then reduced with a selective reducing agent, for example sodium cyanoborohydride, to give the compounds of the invention directly .....

Also in Nofre et al, at column 7, lines 39-51, there is given an example showing that 3,3-dimethylbutyl derivative is reduced in methanol with sodium cyanoborohydride.

Such reduction methods described in Nofre et al are called "hydride reductions." There is no disclosure or suggestion of any method other than reduction with sodium cyanoborohydride, that is, the hydride reduction, in Nofre et al. Moreover, the only example in this reference uses 3,3-dimethylbutyl aldehyde and sodium cyanoborohydride.

On the other hand, as the Examiner will note, present Claim 1 has been amended to recite "wherein said reductive alkylation comprises catalytic hydrogenation." Since there is

no disclosure or suggestion of catalytic hydrogenation reaction in Nofre et al, the rejection is improper and should be withdrawn.

The rejection of Claims 23-26 under 35 U.S.C. § 102(b) in view of Nofre et al is respectfully traversed. At column 7, lines 48-51 of Nofre et al, there is found a description showing that the 3,3-dimethylbutyl derivative has been crystallized in the solvent of ethanol/water or acetonitrile. However, this reference does not describe that a series of the compounds can be purified with the same or similar crystallization method and/or with the same solvent. Further, with respect to the compound 18 shown in the Table 1 of Nofre et al, this reference does not describe even the following:

(1) How the compound has been purified (how to purify);

(2) Whether or not the compound can be isolated in the crystalline form; or

(3) Even if the compound exists as a crystalline form.

Since there is no disclosure of crystalline N-[N-[3-(3-methoxy-4-hydroxyphenyl)propyl]-L-α-aspartyl]-L-phenylalanine 1-methyl ester, this reference cannot anticipate any of Claims 23-26. Moreover, since there is no disclosure of how to purify N-[N-[3-(3-methoxy-4-hydroxyphenyl)propyl]-L-α-aspartyl]-L-phenylalanine 1-methyl ester or whether N-[N-[3-(3-methoxy-4-hydroxyphenyl)propyl]-L-α-aspartyl]-L-phenylalanine 1-methyl ester even exists in the crystalline state, this reference cannot make Claims 23-26 obvious.

Accordingly, the rejection should be withdrawn.

Thus, the present invention is neither disclosed nor suggested in the reference.

The rejection of Claims 27 and 28 under 35 U.S.C. § 102(b) in view of Nofre et al is respectfully traversed. As explained above Claim 23 is fully patentable over Nofre et al. Claims 27 and 28 recite the presence of the crystalline N-[N-[3-(3-methoxy-4-

hydroxyphenyl)propyl]-L-α-aspartyl]-L-phenylalanine 1-methyl ester of Claim 23. Thus, Claims 27 and 28 are patentable over Nofre et al for at least the same reasons that Claim 23 is patentable over this reference. Thus, the rejection should be withdrawn.

The rejection of Claims 15, 17, 18, 20, and 30 under 35 U.S.C. § 103(a) in view of Nofre et al and further in view of U.S. Patent No. 5,510,508 (Claude et al) is respectfully traversed. As explained above, Nofre et al only discloses reductive alkylation reaction with sodium cyanoborohydride. On the other hand, Claude et al discloses catalytic hydrogenation with platinum using only 3,3-dimethylbutyl aldehyde as the aldehyde.

Apparently, it is the Examiner's position that it would have been obvious to apply the catalytic hydrogenation of Claude et al to the preparation of compound no. 18 of Nofre et al. However, ***the combination of catalytic hydrogenation using Pd-carbon or the like with an aldehyde derivative having an aromatic ring as in the present invention is neither disclosed nor suggested in these references***. In fact, these references actually would lead one of skill in art away from the presently claimed methods. Specifically, in Claude et al, at column 3, lines 21-26, it is disclosed that catalytic hydrogenation with hydrogen and other metal catalysts gives rise to a secondary reaction (formation of by-product), such as a reduction of the aromatic ring in Aspartame (reduction of the aromatic nucleus).

Moreover, the fact that Claude et al only discloses application of the Pd-carbon catalyst to the production of Neotame, i.e., the 3,3-dimethylbutyl derivative, suggests that the use of catalytic hydrogenation with the Pd-carbon catalyst can not be applied to the present invention. That is, based on the disclosure of Claude et al, a person skilled in the art would have believed that in case of the presently claimed method using the aldehyde which contains

an aromatic ring, such catalytic hydrogenation reaction would not proceed well but would instead give rise to side reactions involving reduction of the aromatic ring.

For all of these reasons, the rejection should be withdrawn.

The rejection of Claims 7, 10-12, 33, 36, and 37 under 35 U.S.C. § 103(a) in view of Nofre et al and further in view of U.S. Patent No. 6,077,962 (Prakash et al) is respectfully traversed. The disclosure of Nofre et al is discussed above. Prakash et al is directed to toward the synthesis of Neotame and completely unconcerned with N-[N-[3-(3-methoxy-4-hydroxyphenyl)propyl]-L-α-aspartyl]-L-phenylalanine 1-methyl ester. Thus, there is simply no disclosure in any of the cited references with respect to relevant properties of (1) the compound produced by the presently claimed method; and (2) the aldehyde starting materials used in the presently claimed; *i.e.*, there is no disclosure of their solubilities in various solvents, or even whether or not such compounds or starting materials can be dissolved in the particular solvent for extraction. Regarding the solubilities thereof in the solvents, it is difficult to predict the possibilities whether or not the compounds in the present invention would have the same properties as such above 3,3-dimethylbutyl derivative in the references. Accordingly, one of skill in the art would not have had a reasonable expectation of success for applying the disclosure of Prakash et al to the production and/or purification of N-[N-[3-(3-methoxy-4-hydroxyphenyl)propyl]-L-α-aspartyl]-L-phenylalanine 1-methyl ester.

Thus, the rejection should be withdrawn.

The rejection of Claim 29 under 35 U.S.C. § 103(a) in view of Nofre et al and Claude et al and further in view of Solomons is respectfully traversed. The disclosures of Nofre et al and Claude et al have been discussed above. Solomons only discloses the catalytic hydrogenation reaction for hydrocarbons (alkene). In contrast, the present method invloves

the use of starting materials which are much more complicated from the perspective of functional groups. Accordingly, the method of Solomons can not be applied to the present invention.

As explained in the present specification, in the catalytic hydrogenation reaction of the compounds of the cinnamaldehyde type (i.e., those compounds having an aromatic ring, a carbon-carbon double bond, and conjugated carbonyl group), the reduction of the aldehyde to form an alcohol is also generated together with a reduction of the carbon-carbon double bond, and these reactions compete with the reduction of the imine which is formed in the system of reaction. In such case, the corresponding alcohol is generated and formed as a result of the competing side reaction, and therefore any analogy from the reaction system disclosed in Solomon can not be applied to the present invention.

In support of the assertion that one of skill in the art would have recognized the complications of applying catalytic hydrogenation to such starting materials, Applicants cite: (1) S. Nishimura, Handbook of Heterogeneous Catalytic Hydrogenation for Organic Synthesis, John Wiley & Sons, NY, pp. 178-185, 2001; and (2) T. Fukuda, Nippon Kagaku Zasshi, vol. 83, pp. 1126-1129 (1962), Chem. Abstracts, 59:11310e, 1963. In these publications, the results of the catalytic reduction of cinnamaldehyde with various catalysts are reported. With the palladium-based catalyst, reduction of the C-C double bond and the carbonyl group and removal of the CO occur to produce β-phenyl propionaldehyde, cinnamyl alcohol, styrene, and carbon monoxide. Thus, the cinnamyl alcohol formed is decomposed through hydrogenolysis.

With the Raney Nickel catalyst, reduction of the C-C double bond and removal of the CO occur, and β-phenyl propionaldehyde is hydrogenated to form 3-phenyl-1-propanol.

With the platinum-based catalyst, the same reactions as in the case of the palladium-based catalyst occur, and the final products are the same as in the case of the palladium-based catalyst.

It is the surprising discovery of the present inventors that despite the fact that the reduction of the aldehyde to an alcohol can be proceed as a competitive reaction, the desired products can nonetheless be obtained in the present invention. These findings are novel and new and unexpected. Simply put, there is nothing in any of the cited references which would suggest the ability to apply catalytic hydrogenation to a system containing an unsaturated aldehyde, such as an aldehyde having a carbon-carbon double bond, as in the presently claimed method.

For these reasons, the rejection should be withdrawn.

The rejections of claims under 35 U.S.C. § 112, second paragraph, has been, in part, obviated by appropriate amendment and is, in part, respectfully traversed. As the Examiner will note, Applicants have amended the claims such that they are free of most of the criticisms outlined on pages 3-6 of the Official Action. However, in regard to paragraph nos. 7 and 12 on pages 4 and 5 of the Official Action, Applicants note that a claim is definite if one of skill in the art can ascertain whether it is infringed. Applicants submit that one of skill in the art would have no problem determining whether a method contained a crystallization step (paragraph no. 7) of whether a starting material contained a protected-hydroxy group (paragraph no. 12). Accordingly, the rejection should be withdrawn.

The rejection of Claim 1-3, 5, 6, 8-10, 13, 14, 26, 31-34, 38, and 39 under 35 U.S.C. § 112, first paragraph, is respectfully traversed. To meet the enablement requirement, need to disclosed only one mode for carrying out the claimed invention without undue

experimentation. In the present case, the specification provides a detailed discussion, including examples, of the crystallization of N-[N-[3-(3-methoxy-4-hydroxyphenyl)propyl]-L-α-aspartyl]-L-phenylalanine 1-methyl ester. Accordingly, one of skill in the art would clearly be able to carry out the crystallization step without undue experimentation. Thus, the rejection should be withdrawn.

The objection to the specification has been obviated by appropriate amendment. As the Examiner will note, Applicants have amended page 1 of the specification as suggested on page 2 of the Official Action.

The objection to Claim 25 under 37 C.F.R. § 1,75(c) has been obviated by the cancellation of this claim.

Applicants submit that the application is now in condition for allowance, and early notification of such action is earnestly solicited.

Respectfully submitted,

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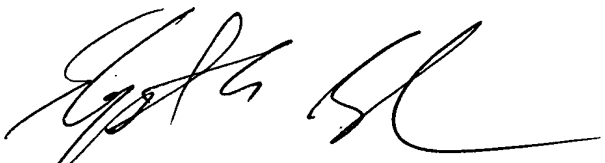

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MARKED-UP COPY OF AMENDMENT FILED HEREWITH

IN THE SPECIFICATION

Please amend the specification as shown on the attached marked-up copy to read as follows:

Page 1, line 2, delete "TITLE OF THE INVENTION";

on a new line, after line 5, please insert the following new paragraph:

--CROSS REFERENCES TO RELATED APPLICATIONS

This application is a continuation of PCT JP00/05665, which was filed August 23, 2000, and which is incorporated herein by reference in its entirety.--

IN THE CLAIMS

Please amend the claims as shown on the attached marked-up copy to read as follows.

--1. (Amended) A method for producing N-[N-[3-(3-methoxy-4-hydroxyphenyl)propyl]-L-α-aspartyl]-L-phenylalanine 1-methyl ester, comprising:

(1) subjecting [Aspartame] N-L-α-aspartyl-L-phenylalanine 1-methyl ester and 3-(3-methoxy-4-hydroxyphenyl)propionaldehyde or [derivatives] a derivative thereof to reductive alkylation in a solvent to [produce] obtain N-[N-[3-(3-methoxy-4-hydroxyphenyl)propyl]-L-α-aspartyl]-L-phenylalanine 1-methyl ester; and

(2) crystallizing said [compound] N-[N-[3-(3-methoxy-4-hydroxyphenyl)propyl]-L-α-aspartyl]-L-phenylalanine 1-methyl ester,

wherein said reductive alkylation comprises catalytic hydrogenation, and

wherein said derivative thereof is selected from the group consisting of

3-(3-methoxy-4-hydroxyphenyl)-2-propenylaldehyde,

3-(3-methoxy-4-protected-hydroxyphenyl)propionaldehyde,

3-(3-methoxy-4-protected-hydroxyphenyl)-2-propenylaldehyde, and

acetals derived therefrom.

2. (Amended) The method [as defined in] of Claim 1, wherein [the] said [process for] crystallizing said [compound] N-[N-[3-(3-methoxy-4-hydroxyphenyl)propyl]-L-α-aspartyl]-L-phenylalanine 1-methyl ester comprises any one of the following crystallization methods:

a. crystallization with a solvent useful for crystallization;

b. crystallization after extraction with water; and

c. crystallization after separation of [Aspartame] N-L-α-aspartyl-L-phenylalanine 1-methyl ester.

3. (Amended) A method for purifying N-[N-[3-(3-methoxy-4-hydroxyphenyl)propyl]-L-α-aspartyl]-L-phenylalanine 1-methyl ester, which comprises:

subjecting a composition which comprises N-[N-[3-(3-methoxy-4-hydroxyphenyl)propyl]-L-α-aspartyl]-L-phenylalanine 1-methyl ester and [comprising] at least one compound selected from the group consisting of [Aspartame] N-L-α-aspartyl-L-phenylalanine 1-methyl ester, a peptide derivative, an amino acid, an amino acid derivative,

an aldehyde, an acetal and an alcohol derivative as impurity to at least any one of the following crystallization processes:

a. crystallization with a crystallization solvent;

b. crystallization after extraction with water; and

c. [in the instance Aspartame is present,] when said composition comprises N-L-α-aspartyl-L-phenylalanine 1-methyl ester, further crystallization after [Aspartame] said N-L-α-aspartyl-L-phenylalanine 1-methyl ester has been separated,

to [crystallize said compound] obtain crystalline N-[N-[3-(3-methoxy-4-hydroxyphenyl) propyl]-L-α-aspartyl]-L-phenylalanine 1-methyl ester.

4. (Amended) The method [as defined in] of Claim 1, wherein [the] said solvent for [the] said reductive alkylation reaction is at least one solvent selected from the group consisting of [alcohol(s)] alcohols, tetrahydrofuran, acetonitrile, toluene, acetic acid, [and] acetic acid [ester(s)] esters, [or a] and mixed [solvent] solvents which [consists of] comprise at least one of these organic solvents and water.

5. (Amended) The method [as claimed in] of Claim 2, wherein said [compound] N-[N-[3-(3-methoxy-4-hydroxyphenyl) propyl]-L-α-aspartyl]-L-phenylalanine 1-methyl ester is crystallized by a process of concentration or by a process for solvent substitution.

6. (Amended) The method [as claimed in] of Claim 1, wherein [the] said solvent for said crystallization of said [compound] N-[N-[3-(3-methoxy-4-hydroxyphenyl) propyl]-L-α-aspartyl]-L-phenylalanine 1-methyl ester is at least one solvent selected from the group consisting of [alcohol(s)] alcohols, tetrahydrofuran, acetonitrile, toluene, ether, acetone, acetic acid, [and] acetic acid [ester(s)] esters, [or a] and mixed [solvent] solvents which [consists of] comprise at least one of these organic solvents and water.

7. (Amended) The method [as claimed in] of Claim 1, wherein [the] said solvent for said crystallization of said [compound] N-[N-[3-(3-methoxy-4-hydroxyphenyl) propyl]-L-α-aspartyl]-L-phenylalanine 1-methyl ester [comprises a] is the same solvent which has been used in the reductive alkylation reaction.

8. (Amended) The method [as claimed in] of Claim 5, wherein [the solvent of the substitution aspect of crystallization is] said N-[N-[3-(3-methoxy-4-hydroxyphenyl)propyl]-L-α-aspartyl]-L-phenylalanine 1-methyl ester is crystallized by solvent substitution using at least one solvent selected from the group consisting of [alcohol(s)] alcohols, tetrahydrofuran, acetonitrile, toluene, ether, acetone, acetic acid, [and] acetic acid [ester(s)] esters, [or a] and mixed [solvent] solvents which [consists of] comprise at least one of these organic solvents and water.

9. (Amended) The method [as claimed in] of Claim 1, wherein [the] said solvent of [the] said reductive alkylation reaction is [alcohol(s)] one or more alocohols or a mixed solvent of [alcohol(s)] one or more alcohols and water, and the solvent of [the] said crystallization [process] of [the compound] said N-[N-[3-(3-methoxy-4-hydroxyphenyl)propyl]-L-α-aspartyl]-L-phenylalanine 1-methyl ester is [alcohol(s)] one or more alcohols or a mixed solvent comprising [alcohol(s)] one or more alcohols.

10. (Amended) The method [as claimed in] of Claim 2, wherein [the solvent of crystallization] said N-[N-[3-(3-methoxy-4-hydroxyphenyl)propyl]-L-α-aspartyl]-L-phenylalanine 1-methyl ester is crystallized after extraction with water [is] using at least one solvent selected from the group consisting of [alcohol(s)] alcohols, tetrahydrofuran, acetonitrile, toluene, ether, acetone, acetic acid, [and] acetic acid [ester(s)], and [or a] mixed

[solvent] solvents which [consists of] comprise at least one of these organic solvents and water.

11. (Amended) The method [as claimed in] of Claim 2, wherein said N-[N-[3-(3-methoxy-4-hydroxyphenyl)propyl]-L-α-aspartyl]-L-phenylalanine 1-methyl ester is crystallized after extraction with water and said [the process for] extraction with water is conducted with a mixed solvent which [consists of] comprises water and one or more organic [solvent(s)] solvents, wherein said [the] organic solvent [forming] forms a layer which separates from an aqueous layer upon mixture with water, and said N-[N-[3-(3-methoxy-4-hydroxyphenyl) propyl]-L-α-aspartyl]-L-phenylalanine 1-methyl ester [being] is extracted into the aqueous layer.

12. (Amended) The method [as claimed in] of Claim 11, wherein said organic [solvent(s)] solvent is at least one solvent selected from the group consisting of acetic acid [ester(s)] esters, ether, chloroform, dichloromethane, hexane, toluene, [alcohol(s)] alcohols, tetrahydrofuran, acetone, acetonitrile and acetic acid.

13. (Amended) The method [as claimed in] of Claim 2, wherein [the solvent for said crystallization] said N-[N-[3-(3-methoxy-4-hydroxyphenyl)propyl]-L-α-aspartyl]-L-phenylalanine 1-methyl ester is crystallized after having separated [Aspartame] N-L-α-aspartyl-L-phenylalanine 1-methyl ester and is crystallized from [is] at least one solvent selected from the group consisting of [alcohol(s)] alcohols, tetrahydrofuran, acetonitrile, toluene, ether, acetone, acetic acid, [and] acetic acid [ester(s)] esters, [or a] and mixed [solvent] solvents which [consists of] comprise at least one of these organic solvents and water.

14. (Amended) The method [as claimed in] of Claim 2, wherein said process for separating [Aspartame] N-L-α-aspartyl-L-phenylalanine 1-methyl ester is a process for separating [Aspartame] N-L-α-aspartyl-L-phenylalanine 1-methyl ester by crystallization or precipitation with at least one solvent selected from the group consisting of acetic acid [ester(s)] esters, ether, chloroform, dichloromethane, hexane, toluene, [alcohol(s)] alcohols, tetrahydrofuran, acetone, acetonitrile, acetic acid and water.

15. (Amended) The method [as claimed in] of Claim 1, wherein said reductive alkylation reaction is conducted in [the presence of hydrogen and a catalyst for reductive alkylation, and the solvent for said reaction is] at least one organic solvent which dissolves the starting materials or a mixed solvent of said organic solvents and water, and when an insoluble material is present in the reaction mixture obtained after said reductive alkylation reaction, said insoluble material is separated by filtration.

17. (Amended) The method [as claimed in] of Claim 1, wherein [the catalyst for said reductive alkylation reaction is a] said catalytic hydrogenation [catalyst and] is conducted in the presence of at least one catalyst selected from the group consisting of palladium, platinum, and rhodium based catalysts.

18. (Amended) The method [as claimed in] of Claim 1 [15], wherein said catalytic hydrogenation is conducted at a hydrogen [is present at a] pressure of 0.1 to 1 MPa.

19. (Amended) The method [as claimed in] of Claim 1, wherein[, in] said reductive alkylation reaction[, the reaction] is conducted at a temperature [ranges] range of from 15 to 50 °C, and [the] a reaction time [ranges] of from 2 to 48 hours.

20. (Amended) The method [as claimed in] of Claim 1, wherein [the pH of the reaction solvent for] said reductive alkylation reaction [ranges] is carried out in a reaction solvent having a pH of from 4 to 6.5.

21. (Amended) The method [as claimed in] of Claim 1, wherein the molar ratio of [the Aspartame] said N-L-α-aspartyl-L-phenylalanine 1-methyl ester to said 3-(3-methoxy-4-hydroxyphenyl)propionaldehyde or derivative thereof ranges from 0.5 to 2.

22. (Amended) The method [as claimed in] of Claim 3, wherein said aldehyde is selected from the group consisting of:

3-(3-methoxy-4-hydroxyphenyl)propionaldehyde,

3-(3-methoxy-4-hydroxyphenyl)-2-propenylaldehyde,

3-(3-methoxy-4-protectedhydroxyphenyl)propionaldehyde,

3-(3-methoxy-4-protectedhydroxyphenyl)-2-propenylaldehyde,

and said acetal comprises any acetal derived from these aldehydes.

23. (Amended) [A] Crystalline N-[N-[3-(3-methoxy-4-hydroxyphenyl)propyl]-L-α-aspartyl]-L-phenylalanine 1-methyl ester [in the crystalline form], which is prepared by the process of Claim 1.

24. (Amended) [A] Crystalline N-[N-[3-(3-methoxy-4-hydroxyphenyl)propyl]-L-α-aspartyl]-L-phenylalanine 1-methyl ester [in crystalline form], which exhibits X-ray diffraction peaks [in at least] at 2θ diffraction angles of 5.55°, 12.25°, 18.5°, 21.1° and 22.45° with CuKα rays [(2θ, CuKα ray)].

26. (Amended) The crystalline N-[N-[3-(3-methoxy-4-hydroxyphenyl)propyl]-L-α-aspartyl]-L-phenylalanine 1-methyl ester [compound as claimed in] of Claim 23, which is obtained upon crystallization of N-[N-[3-(3-methoxy-4-hydroxyphenyl)propyl]-L-α-aspartyl]-

L-phenylalanine 1-methyl ester [said compound] from at least one solvent selected from the group consisting of [alcohol(s)] alcohols, tetrahydrofuran, acetonitrile, toluene, ether, acetone, acetic acid, [and] acetic acid [ester(s)] esters, [or a] and mixed [solvent] solvents which [consists of] comprise at least one of these organic solvents and water.

27. (Amended) A sweetening agent, a food and drink, a medicament, a confectionary, a hygienic article, or a sweetened food and drink for mammals comprising [the compound as claimed in] said crystalline N-[N-[3-(3-methoxy-4-hydroxyphenyl)propyl]-L-α-aspartyl]-L-phenylalanine 1-methyl ester of Claim 23.

28. (Amended) A sweetener comprising [the compound] said crystalline N-[N-[3-(3-methoxy-4-hydroxyphenyl)propyl]-L-α-aspartyl]-L-phenylalanine 1-methyl ester of Claim 23 and at least one adjunct selected from the group consisting of a carrier, a bulking agent and excipient, which is employed in sweetening materials.

29. (Amended) The method [as claimed in] of Claim 1, wherein said 3-(3-methoxy-4-hydroxyphenyl) propionaldehyde or derivative thereof is prepared by subjecting 3-(3-methoxy-4-hydroxyphenyl)-2-propenylaldehyde or an acetal thereof, wherein the hydroxyl group may be protected, to reduction to [reduce the double bond of the compound] obtain said 3-(3-methoxy-4-hydroxyphenyl) propionaldehyde or derivative thereof.

30. (Amended) The method [as defined in] of Claim [28] 29, wherein said [process for] reduction is conducted in the presence of a reduction catalyst or a rhodium based catalyst.

31. (Amended) The method [as claimed in] of Claim 3, wherein said [compound] N-[N-[3-(3-methoxy-4-hydroxyphenyl)propyl]-L-α-aspartyl]-L-phenylalanine 1-methyl ester is crystallized by a process of concentration or by a process for solvent substitution.

32. (Amended) The method [as claimed in] of Claim 3, wherein [the solvent for] said crystallization of said [compound] N-[N-[3-(3-methoxy-4-hydroxyphenyl)propyl]-L-α-aspartyl]-L-phenylalanine 1-methyl ester is carried out in at least one solvent selected from the group consisting of [alcohol(s)] alcohols, tetrahydrofuran, acetonitrile, toluene, ether, acetone, acetic acid, [and] acetic acid [ester(s)] esters, [or a] and mixed [solvent] solvents which [consists of] comprise at least one of these organic solvents and water.

33. (Amended) The method [as claimed in] of Claim 2, wherein [the solvent for] said crystallization of said [compound comprises] N-[N-[3-(3-methoxy-4-hydroxyphenyl)propyl]-L-α-aspartyl]-L-phenylalanine 1-methyl ester is carried out in the same [a] solvent which has been used in [the] said reductive alkylation reaction.

34. (Amended) The method [as claimed in] of Claim 31, wherein [the] said N-[N-[3-(3-methoxy-4-hydroxyphenyl)propyl]-L-α-aspartyl]-L-phenylalanine 1-methyl ester is crystallized by solvent [of the] substitution [aspect of crystallization is] using at least one solvent selected from the group consisting of [alcohol(s)] alcohols, tetrahydrofuran, acetonitrile, toluene, ether, acetone, acetic acid, [and] acetic acid [ester(s)] esters, [or a] and mixed [solvent] solvents which [consists of] comprise at least one of these organic solvents and water.

35. (Amended) The method [as claimed in] of Claim 2, wherein [the] said solvent of the reductive alkylation reaction is [alcohol(s)] one or more alcohols or a mixed solvent of [alcohol(s)] one or more alcohols and water, and the solvent of the crystallization [process] of [the compound] said N-[N-[3-(3-methoxy-4-hydroxyphenyl)propyl]-L-α-aspartyl]-L-phenylalanine 1-methyl ester is [alcohol(s)] one or more alcohols or a mixed solvent comprising [alcohol(s)] one or more alcohols.

36. (Amended) The method [as claimed in] of Claim 3, wherein [the solvent of crystallization] said N-[N-[3-(3-methoxy-4-hydroxyphenyl)propyl]-L-α-aspartyl]-L-phenylalanine 1-methyl ester is crystallized after extraction with water [is] using at least one solvent selected from the group consisting of [alcohol(s)] alcohols, tetrahydrofuran, acetonitrile, toluene, ether, acetone, acetic acid, [and] acetic acid [ester(s)] esters, [or a] and mixed [solvent] solvents which [consists of] comprise at least one of these organic solvents and water.

37. (Amended) The method [as claimed in] of in Claim 3, wherein said N-[N-[3-(3-methoxy-4-hydroxyphenyl)propyl]-L-α-aspartyl]-L-phenylalanine 1-methyl ester is crystallized after extraction with water and said [the process for] extraction with water is conducted with a mixed solvent which [consists of] comprises water and one or more organic [solvent(s)] solvents, wherein said [the] organic solvent [forming] forms a layer which separates from an aqueous layer upon mixture with water, and said N-[N-[3-(3-methoxy-4-hydroxyphenyl) propyl]-L-α-aspartyl]-L-phenylalanine 1-methyl ester [being] is extracted into the aqueous layer.

38. (Amended) The method [as claimed in] of Claim 3, wherein [the solvent for said crystallization] said N-[N-[3-(3-methoxy-4-hydroxyphenyl)propyl]-L-α-aspartyl]-L-phenylalanine 1-methyl ester is crystallized after having separated [Aspartame] N-L-α-aspartyl-L-phenylalanine 1-methyl ester and is crystallized from [is] at least one solvent selected from the group consisting of [alcohol(s)] alcohols, tetrahydrofuran, acetonitrile, toluene, ether, acetone, acetic acid, [and] acetic acid [ester(s)] esters, [or a] and mixed [solvent] solvents which [consists of] comprise at least one of these organic solvents and water.

39. (Amended) The method [as claimed in] of Claim 3, wherein said process for separating [Aspartame] N-L-α-aspartyl-L-phenylalanine 1-methyl ester is a process for separating [Aspartame] N-L-α-aspartyl-L-phenylalanine 1-methyl ester by crystallization or precipitation with at least one solvent selected from the group consisting of acetic acid [ester(s)] esters, ether, chloroform, dichloromethane, hexane, toluene, [alcohol(s)] alcohols, tetrahydrofuran, acetone, acetonitrile, acetic acid and water.--

Please cancel Claims 16 and 25, without prejudice toward the further prosecution of this claim in a continuation and/or divisional application.